

alternative means of abortive therapy even if they need to continue to carry an intramuscular epinephrine injector for severe episodes.

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Single-dose oral dexamethasone is effective in preventing relapse after acute asthma exacerbations



Acute asthma exacerbations are a common cause for emergency department (ED) visits and the most frequent reason for childhood hospitalization in the United States.^{1,2} Asthma care guidelines recommend systemic corticosteroids for the management of acute exacerbations and prevention of relapse.³ However, for children with Medicaid insurance, corticosteroid prescriptions are filled in fewer than 45% of instances after ED discharge.⁴ Single-dose dexamethasone circumvents this noncompliance and the need for multiday regimens of prednisone or prednisolone, and small randomized controlled trials have suggested that dexamethasone works as well as prednisone and prednisolone in ED settings.⁵ Our objective was to examine relapse rates in a large population of children treated for acute asthma exacerbations during an era of prednisone and prednisolone use compared with an era of dexamethasone use.

The study protocol was reviewed and approved by the institutional review board of Vanderbilt University (Nashville, Tennessee). Data were extracted from electronic medical records of all patients 3 to 17 years old presenting to our urban, tertiary care children's hospital ED from January 2006 through December 2014 with a primary *International Classification of Diseases, Ninth Revision* code (493.00) for acute asthma. We identified patients seen in the ED, treated with systemic corticosteroids, and subsequently discharged. Within that group, we identified those who returned within 72 hours for continued asthma symptoms. For patients with multiple ED visits within 72 hours, only the first return visit was analyzed to avoid double counting of patients. The institutional practice guideline transitioned from 2 mg/kg of prednisone or prednisolone for 3 to 5 days to single-dose dexamethasone (0.6 mg/kg, maximum 16 mg) in the spring of 2014. The children's hospital asthma steering committee chose to maximize the dose of dexamethasone to minimize the likelihood of treatment failure. This dose of dexamethasone is approximately twice as potent as a 2 mg/kg dose of daily prednisone or prednisolone; however, as a long-acting corticosteroid, its effects last up to 3 days.⁶

The χ^2 test was used to compare relapse rates of patients receiving oral dexamethasone with those receiving oral prednisone or prednisolone, and multivariable logistic regression was used to examine for associations of corticosteroid formulation with relapse, adjusted for sex, age, race, ethnicity, and insurance type.

Of 13,518 unique patient ED visits for asthma, there were 183 (1.4%) with relapse. Patient demographics are presented in Table 1. Data from 4,749 patients (35.1%) who received no corticosteroid or an intravenous formulation of corticosteroid were

not included in the analysis. We identified 7,130 patients (52.7%) who received oral prednisone or prednisolone and 1,639 (12.1%) who received oral dexamethasone. There were 143 relapses (2.01%) in patients receiving oral prednisone or prednisolone and 21 (1.28%) in those receiving oral dexamethasone ($P = .05$, absolute risk reduction 0.73%, relative risk reduction 36%). No demographic characteristics were associated with relapse in multivariable models.

To our knowledge, this is the first large, pragmatic, real-world analysis examining the choice of corticosteroid preparation with relapse rates, a critical outcome in ED asthma therapy. Our results indicate that single-dose oral dexamethasone is associated with a decrease of ED relapse for pediatric patients with acute asthma exacerbations. Study limitations include lack of information regarding the severity of a patient's asthma exacerbation and detailed asthma characteristics (eg, intermittent vs persistent, presence of smoke exposure, and influenza vaccination status). In addition, any patient with an incorrect *International Classification of Diseases, Ninth Revision* code not reflective of acute asthma as the primary cause for ED visit was missed in our analysis. Based on our results, dexamethasone may be the

Table 1

Demographic characteristics of patients 3 to 17 years old with acute asthma exacerbations discharged from an urban pediatric emergency department^a

Characteristic	All patients with asthma (N = 13,518)	Patients with relapse (n = 183)
Sex		
Boys	8,281 (61)	109 (60)
Girls	5,237 (39)	74 (40)
Race		
White	4,783 (35)	63 (34)
Black	7,701 (57)	108 (59)
Asian	119 (1)	1 (1)
American Indian or Alaskan	36 (0)	0 (0)
Pacific Islander	1 (0)	0 (0)
Unknown or declined	878 (7)	11 (6)
Ethnicity		
Non-Hispanic	9,055 (67)	141 (77)
Hispanic	1,249 (9)	11 (6)
Unknown or declined	3,214 (24)	31 (17)
Insurance		
Medicaid	8,446 (63)	125 (68)
Commercial	4,479 (33)	55 (30)
Military	152 (1)	1 (1)
Unknown or declined	441 (3)	2 (1)
Age (y), median (interquartile range)	7 (4–10)	7 (4–11)

^aValues are presented as number (percentage) unless otherwise specified.

preferred oral corticosteroid in the ED management of pediatric patients with acute asthma exacerbations.

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Immunoglobulin replacement for selective IgM immunodeficiency, bronchiectasis, and asthma



Selective IgM immunodeficiency (SIgMID) is a primary humoral immunodeficiency characterized by a low serum level of IgM at least 2 SDs below age-adjusted means.¹ Like other primary humoral immunodeficiencies, SIgMID is most commonly associated with recurrent infection, particularly upper and lower respiratory tract infections.^{2–4} SIgMID is also associated with allergic rhinitis, angioedema, anaphylaxis, urticaria, autoimmune diseases, malignant tumors, asthma, and bronchiectasis.⁴

Immunoglobulin supplementation is first-line therapy for common variable immunodeficiency and anecdotally used for other primary humoral immunodeficiencies (ie, specific antibody deficiency [SAD], specific IgA immunodeficiency with and without IgG subclass deficiency [IgGSD], IgGSD with normal quantitative immunoglobulins, and SIgMID).^{3–6} The primary indication for immunoglobulin supplementation in these cases is recurrent infection.⁵

Bronchiectasis is a progressive, destructive airway disease secondary to airway inflammation and infection. There is no effective disease-modifying treatment that reverses the destruction or reduces bronchial damage. Bronchiectasis is traditionally treated acutely and prophylactically with bronchodilators, inhaled corticosteroids, mucolytics, and antibiotics.⁷ Although immunoglobulin supplementation is not used routinely for bronchiectasis, immunoglobulin supplementation at conventional doses (0.3–0.8 g/kg monthly) has been effective in patients with bronchiectasis and common variable immunodeficiency and in patients with IgGSD and bronchiectasis.^{5–7}

Intravenous immunoglobulin (IVIG) has also been used in select cases of asthma.^{8–10} A review of patients with IgGSD and/or SAD with refractory asthma reported clinical response to IVIG at conventional doses with a reduced number of respiratory infections, fewer hospitalizations, and reduced oral corticosteroid use.⁸ IVIG has also been used in patients with corticosteroid-dependent or refractory asthma without history of immunodeficiency. These patients had clinical improvement and reduced oral corticosteroid use while taking anti-inflammatory doses (2 mg/kg monthly) of IVIG.^{9,10}

IVIG has been used effectively at conventional doses in patients with SIgMID and a history of recurrent infections but without

bronchiectasis.³ We hypothesize that immunoglobulin supplementation has the potential to decrease respiratory infections, bronchiectasis flares, and exacerbations of asthma in patients with SIgMID. We report the first use, to our knowledge, of IVIG in patients with SIgMID, bronchiectasis, and asthma.

We performed a retrospective medical record review of 130 patients with SIgMID. Four patients with SIgMID, computed tomography (CT)-confirmed bronchiectasis, and persistent moderate to severe asthma were treated with IVIG. Analysis of upper and lower respiratory tract infections and bronchiectasis flares requiring antibiotics, asthma exacerbations requiring oral corticosteroids, and radiologically confirmed pneumonia before and after IVIG was performed.

Eighteen of 130 patients (14%) had symptomatic and radiographic findings of multilobe bronchiectasis. Fifteen of the 18 patients also had a positive methacholine challenge result at 8 mg/mL or less and symptoms consistent with mild to severe asthma. These patients were treated for asthma in accordance with National Institutes of Health guidelines.¹¹ Four nonsmoking patients (3%) with the triad of bronchiectasis, persistent moderate to severe asthma with positive methacholine challenge results, and SIgMID (mean [SD] IgM level, 27 [9.1] mg/dL) were treated with IVIG because of recurrent upper and/or lower respiratory tract infections and bronchiectasis flares requiring antibiotics, frequent asthma exacerbations requiring oral corticosteroid bursts, and history of pneumonia(s). These 4 patients had been followed up for 2 to 6 years before IVIG treatment. None of the 4 patients had chronic obstructive pulmonary disease, tuberculosis or atypical mycobacteria infections, cystic fibrosis, α_1 -antitrypsin deficiency, allergic bronchopulmonary aspergillosis, inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrome or other causes of bronchiectasis based on radiographic findings, complete pulmonary function test (PFT) results, and laboratory study results. Complete PFTs included spirometry, full lung volume, diffusion capacity, and maximum inspiratory and expiratory pressures. No patients had IgGSD, complement deficiency, human immunodeficiency virus infection, or hematologic abnormalities. One patient had SAD with lack of response to pneumococcal polyvalent vaccine. Three patients consented to anonymous publication of their clinical course; 1 patient was lost to follow-up.

Patients received 2 g/kg monthly of IVIG for 1 year, consistent with anti-inflammatory dosing for refractory asthma.^{9,10} All

Disclosures: Authors have nothing to disclose.

Funding Sources: This study was funded by the Asthma Center Education and Research Fund, a nonprofit education and research foundation (501.c.3) funded through private donations.